

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
11 March 2004 (11.03.2004)

PCT

(10) International Publication Number
WO 2004/020410 A3

(51) International Patent Classification⁷: **C07D 211/90**,
405/04, 401/04, C07F 7/18, A61K 31/4545, A61P 29/00

(21) International Application Number:
PCT/EP2003/009108

(22) International Filing Date: 18 August 2003 (18.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0219894.3 27 August 2002 (27.08.2002) GB
0221143.1 12 September 2002 (12.09.2002) GB

CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

Published:

— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(71) Applicant (*for all designated States except US*): **BAYER HEALTHCARE AG** [DE/DE]; 51368 Leverkusen (DE).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **GIELEN, Heike** [DE/DE]; Am Kettmersbusch 3, 51379 Leverkusen (DE). **MIN-JIAN LI, Volkhart** [DE/DE]; Im Wiesengrund 40, 42553 Velbert (DE). **ROSENTERER, Ulrich** [DE/DE]; Obere Rutenbeck 6, 42349 Wuppertal (DE). **SCHLEMMER, Karl-Heinz** [DE/DE]; Wildsteig 22 a, 42113 Wuppertal (DE). **ALLERHEILIGEN, Swen** [DE/DE]; Beckumsfeld 4, 45259 Essen (DE). **TELAN, Leila** [US/DE]; Rabenweg 42, 42115 Wuppertal (DE). **BÄRFACKER, Lars** [DE/DE]; Bachstr. 98, 46149 Oberhausen (DE). **KELDENICH, Jörg** [DE/DE]; Damaschkeweg 49, 42113 Wuppertal (DE). **FITZGERALD, Mary, F.** [GB/GB]; 2 Paternoster Court, Cassington Road, Yarnton, Oxfordshire OX5 1QB (GB). **NASH, Kevin** [GB/GB]; 136 a Littlebrook ave., Burnham, Slough, Berkshire SL2 2NE (GB). **ALBRECHT, Barbara** [DE/DE]; Heidestr. 9, 42489 Wülfrath (DE). **MEURER, Dirk** [DE/DE]; Platanenweg 1A, 50259 Pulheim (DE).

(74) Common Representative: **BAYER HEALTHCARE AG**; Law and Patents, Patents and Licensing, 51368 Leverkusen (DE).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

(88) Date of publication of the international search report:
22 April 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DIHYDROPYRIDINONE DERIVATIVES AS HNE INHIBITORS

(57) Abstract: The invention relates to novel dihydropyridinone derivatives, processes for their preparation, and their use in medicaments, especially for the treatment of chronic obstructive pulmonary diseases, acute coronary syndrome, acute myocardial infarction and heart failure development.

WO 2004/020410 A3

BEST AVAILABLE COPY

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/09108

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D211/90 C07D405/04 C07D401/04 C07F7/18 A61K31/4545
A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07F A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 925 395 A (BOSSERT FRIEDRICH ET AL) 9 December 1975 (1975-12-09) the whole document	1,13,15, 18,21
A	WO 02/053541 A (BENNEKER FRANCISCUS BERNARDUS ; LEMMENS JACOBUS MARIA (NL); BIOORG B V) 11 July 2002 (2002-07-11) the whole document	1,13,15, 18,21

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

26 February 2004

Date of mailing of the international search report

11/03/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5618 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Diederer, J

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/09108

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 21 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/09108

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3925395	A	09-12-1975	DE 2242787 A1 14-03-1974
			AT 327902 B 25-02-1976
			AT 760073 A 15-05-1975
			AU 476373 B2 16-09-1976
			AU 5983573 A 06-03-1975
			BE 804161 A1 28-02-1974
			CA 1016946 A1 06-09-1977
			CH 592061 A5 14-10-1977
			DD 109628 A5 12-11-1974
			DK 131855 B 15-09-1975
			ES 418340 A1 16-03-1976
			FR 2197598 A1 29-03-1974
			GB 1389505 A 03-04-1975
			HU 167992 B 28-02-1976
			IE 38141 B1 04-01-1978
			IL 43080 A 31-01-1977
			JP 1081810 C 29-01-1982
			JP 49062483 A 17-06-1974
			JP 56026661 B 19-06-1981
			LU 68325 A1 30-10-1973
			NL 7311832 A 04-03-1974
			PL 89430 B1 30-11-1976
			SE 385882 B 26-07-1976
			US 3951992 A 20-04-1976
			US 3951991 A 20-04-1976
			US 3987176 A 19-10-1976
			US 3951990 A 20-04-1976
			US 3981882 A 21-09-1976
			ZA 7305973 A 30-10-1974
WO 02053541	A	11-07-2002	BE 1014451 A6 07-10-2003
			BR 0116554 A 03-02-2004
			CA 2433193 A1 11-07-2002
			DE 20115218 U1 24-01-2002
			EP 1309554 A1 14-05-2003
			WO 02053541 A1 11-07-2002
			US 2003204093 A1 30-10-2003
			US 2002123518 A1 05-09-2002